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10/564,166

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Valerio Berdini

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11/25/2009

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EXAMINER

STOCKTON, LAURA LYNNE

ART UNIT

PAPER NUMBER

1626

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/564,166	<b>Applicant(s)</b> BERDINI ET AL.	
	<b>Examiner</b> Laura L. Stockton	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 September 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 57-98 is/are pending in the application.
- 4a) Of the above claim(s) 57-71, 86-95, 97 and 98 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 72-85 and 96 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>August 7, 2006 and July 16, 2009</u> . | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

**Claims 57-98 are pending in the application.**

***Election/Restrictions***

Applicant's election without traverse of Group V (Claims 72-85 and 96 - drawn to products of formula IV, formula V, formula VI, formula VII and formula VIIa) in the reply filed on September 15, 2009 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Claims 57-71, 86-95, 97 and 98 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 15, 2009.

***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

***Information Disclosure Statement***

The Examiner has considered the Information Disclosure Statements filed on August 7, 2006 and July 16, 2009.

***Specification***

The amendment filed January 3, 2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "The disclosures all of which are hereby incorporated herein by reference in their entirety".

Applicant is required to cancel the new matter in the reply to this Office Action.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 72-85 and 96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a salt or N-oxide of the compounds, does not reasonably provide enablement for a solvate of the compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in making an enablement rejection are summarized as:

- a) the quantity of experimentation necessary,
- b) the amount of direction or guidance presented,
- c) the presence or absence of working examples,
- d) the nature of the invention,
- e) the state of the prior art,
- f) the relative skill of those in the art,
- g) the predictability or unpredictability of the art, and
- h) the breadth of the claims.

In re Colianni, 195 USPQ 150 (CCPA 1977). In re Rainer, et al., 146 USPQ 218 (CCPA 1965). *Ex parte Formal*, 230 USPQ 546 (BPAI 1986).

a) Determining if a particular compound would form a solvate or hydrate would require synthesis and recrystallization of the compound solvate using a variety of solvents, temperatures and humidities. The

experimentation for solvates or hydrates is potentially open-ended.

b) The specification merely mentions the Applicant's intention to make solvates, without teaching the preparation thereof.

c) While the claims recite solvates, no working examples show their formation. As stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ2d 1190, 1194 (Fed.Cir. 1993):

The specification purports to teach, with over fifty examples, the preparation of the claimed compounds ... However ... there is no evidence that such compounds exist ... [T]he examples ... do not produce the postulated compounds ... [T]here is ... no evidence that such compounds even exist.

The specification shows no evidence of the formation and actual existence of solvates and hydrates. Hence, Applicant must show formation of solvates or limit the claims accordingly.

d) The nature of the invention is chemical synthesis of solvates, which involves chemical reactions.

e) The state of the art recognizes that the formation, composition and therapeutic activity of solvates are unpredictable. The Federal Circuit has recognized a solvate as an example of a polymorph or pseudopolymorph (emphasis added):

"Polymorphs" are distinct crystalline structures containing the same molecules. These structural differences can affect various properties of the crystals, such as melting points and hardness (e.g., graphite and diamonds are both crystalline forms of carbon) .... [P]seudopolymorphs are often loosely called polymorphs ... Pseudopolymorphs not only have their molecules arranged differently but also have a slightly different molecular composition. A common type of pseudopolymorph is a solvate, which is a crystal in which the molecules defining the crystal structure "trap" molecules of a solvent. The crystal molecules and the solvent molecules then bond to form an altered crystalline structure.

SmithKline Beecham Corp. v. Apotex Corp., 74 USPQ2d

1398, 1409 (Fed.Cir. 2005). The same rationale obtains



for hydrates; solvates in which the solvent is water. Souillac, et al., Characterization of Delivery Systems, Differential Scanning Calorimetry, pages 217-218 (in Encyclopedia of Controlled Drug Delivery, 1999, John Wiley & Sons, pages 212-227), recognize that different polymorphs of the same drug can have different therapeutic activity (emphasis added):

Because different polymorphic forms of the same drug exhibit significant differences in their physical characteristics, therapeutic activity from one form to another may be different. Studying the polymorphism of a drug and the relative stability of the different polymorphs is a critical part of pre-formulation development.

Further, Vippagunta et al. (Advanced Drug Delivery Reviews, 48 (2001), pages 3-26) state "Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated in to the crystal lattice of a compound is complex and difficult." See page 18, section 3.4.

f) The artisan using Applicant's disclosure to prepare the claimed solvates would be, e.g., an

experienced process chemist with at least a BS chemistry degree.

g) Chemical reactions are known as unpredictable.

In re Marzocchi, et al., 169 USPQ 367, 370 (CCPA 1971);

In re Fisher, 166 USPQ 18, 24 (CCPA 1970). See above regarding the unpredictability of solvate formation.

h) The breadth of the claims includes thousands of compounds of the instant formulas as well as presently unknown compounds embraced by the terms solvates. See MPEP 2164.01(a), discussed supra, justifying the conclusion of lack of enablement commensurate with the claims. Undue experimentation will be required to practice Applicant's claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 74, 77 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 74, "R<sup>1b</sup>-A-NH", "R<sup>1b</sup>-C(=O)NH" and "R<sup>1b</sup>-A-NHC(=O)" all lack antecedent basis from claim 72.

In claim 77, the "R<sup>1a</sup>" definition lacks antecedent from claim 72.

In claim 78, R<sup>6a</sup>-R<sup>9a</sup> representing C<sub>1-8</sub> hydrocarbonyl group substituted by C<sub>1-4</sub> acyloxy lacks antecedent basis from claim 72 {see definition (a)}.

In claim 78, under the definition (a) of R<sup>6a</sup>-R<sup>9a</sup>, the phrase "and R<sup>c</sup>, X<sup>1</sup> and X<sup>2</sup>" is unclear.

In claim 78, under the definition (a) of R<sup>6a</sup>-R<sup>9a</sup>, the adjacent pair of substituents representing "a non aromatic five or six membered ring" lacks antecedent basis because the phrase does not stipulate that the ring must be a heterocyclic ring as found in claim 72.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 72-85 and 96 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-83, 104, 106-115 and 125-127 of copending Application No. 11/813,031. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed compounds are generically claimed in the copending application.

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (C.C.P.A. 1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., treating viral infections).

One skilled in the art would thus be motivated to prepare products embraced by the copending application to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful in treating, for example, viral

infections. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The comparative showing on pages 260-262 of the instant specification has been considered. However, the comparative showing on pages 260-262 is insufficient to overcome the rejection of the instant claims based upon 35 USC 103 over Edwards et al. {WO 2003/035065} as set forth below: because the showing is not commensurate in scope with the instant claims. In re Greenfield, 197 U.S.P.Q. 227 (1978) and In re Lindner, 173 U.S.P.Q. 356 (1972). Also see M.P.E.P.

716.02(d). The instant R<sup>1a</sup> variable definition embraces a plethora of substituents (i.e., cycloalkyl rings; heterocyclic rings, heteroaryl rings; etc.), which substituents are also taught in Edwards et al. Therefore, the showing is not persuasive.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 72-85 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards et al. {WO 2003/035065}.

***Determination of the scope and content of the prior art (MPEP §2141.01)***

Applicant claims 2-(pyrazol-3-yl)benzimidazole compounds. **Edwards et al.** (see entire document; particularly pages 4-9, 26-29, 42-59, 94-199 and 245-247; and especially Compound 248(f) on page 421) teach 2-(pyrazol-3-yl)benzimidazole compounds that are structurally similar to the instant claimed compounds.

***Ascertainment of the difference between the prior art and the claims  
(MPEP §2141.02)***

The difference between the compounds of the prior art and the compounds instantly claimed is that the instant claimed compounds are generically described in the prior art.

***Finding of prima facie obviousness--rational and motivation (MPEP  
§2142-2413)***

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (C.C.P.A. 1964). The motivation to make the claimed compounds derives from the expectation that



structurally similar compounds would possess similar activity (e.g., protein kinase inhibitors).

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful in treating, for example, asthma. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:00 am to 2:30 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either

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Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

/Laura L. Stockton/  
Laura L. Stockton  
Primary Examiner, Art Unit 1626  
Work Group 1620  
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November 25, 2009